

In re Appln. of Benjes et al.  
Application No. 10/615,044

*REMARKS*

*The Present Invention*

The present invention pertains to a process for the preparation of an intermediate useful for preparing kifunensine. The invention also relates to a process for preparing kifunensine.

*The Pending Claims*

Claims 1 and 4-18 are currently pending. Claims 1 and 4-9 are directed to a process for preparing a compound of formula I. Claims 10-18 are directed to a process for preparing kifunensine.

*Amendments to the Claims*

The claims have been amended to point out more particularly and claim more distinctly the present invention. In particular, claim 1 has been amended to recite that the nitrogen protecting group is *N*-acetyl, as supported by the specification at, for example, paragraph [0054]. Claims 6 and 7 have been amended to recite *N*-acetyl-D-mannosamine, as supported by specification at, for example, paragraph [0035]. Claim 8 has been amended to recite 6-*O*-protected-*N*-acetyl-D-mannitol. Support for this amendment is found in the specification at, for example, paragraph [0060].

Claims 2 and 3 have been canceled. No new matter has been added by way of these amendments.

*Summary of the Office Action*

Claims 1-16 and 18 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Claims 1-18 have been rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Kayakiri et al. *Chem. Pharm. Bull.* 1991, 39, 1392-1396 ("Kayakiri I reference"), and Kayakiri et al. *Tetrahedron Lett.* 1990, 31, 225-226 (Kayakiri II reference"). Claims 1-18 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Kayakiri et al. *Chem. Pharm. Bull.* 1991, 39, 1392-1396, in view of Kayakiri et al. *Tetrahedron Lett.* 1990, 31, 225-226. Reconsideration of these rejections is hereby requested.

In re Appln. of Benjes et al.  
Application No. 10/615,044

*Typographical Error in Compound (3) in Publication*

Applicants note that structure of compound 3 is incorrect as it appears in Examples 2-4 of the published application. In particular, compound 3, as it appears in paragraphs [0079], [0081], and [0083] contains an extra methylene unit. The application as filed with the Office does not contain this error.

*Discussion of the Indefiniteness Rejection*

Claims 1-16 and 18 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Specifically, the Office contends that claims 1, 10-11, and 18 fail to recite specific reaction conditions and how the claimed process is performed. In addition, the Office asserts that the claims fail to recite "positive step(s)" of how the process is performed, and rejects to the use of the alleged functional terms "protecting," "removing/removal," "cyclisation," and "preparing" in the claims. This rejection is respectfully traversed as Applicants contend that the claims do recite specific steps of how the process is performed such that one of ordinary skill in the art would understand the metes and bounds of the claims.

The currently pending claims are directed to synthetic processes. To one of ordinary skill in the art, the terms "protecting," "cyclisation," and "removing/removal" refer to fundamental concepts that are well defined in synthetic chemistry. See, for example, Greene, T.W., Wuts, P.G.M., Eds. *Protecting Groups in Organic Synthesis*, 3<sup>rd</sup> ed.; John Wiley & Sons, Inc., 1999, which describes the concept of "protecting" functional groups in organic synthesis and strategies to "remove" protecting groups. Further, "cyclization" is a well known process step in organic synthesis.

These terms are used in the present application in a manner consistent with the way these terms are used and understood by those skilled in the art. For example, the concept of "protecting" functional groups in a molecule with a "protecting group" is described in the specification as "temporarily masking the chemistry of that functional group [with a protecting group] and allowing other sites in the molecule to be manipulated without affecting the functional group" (see paragraph [0044]). The specification also provides specific details on the nature of the protecting groups employed in the claimed invention (see, e.g., paragraphs [0045]-[0052]). Further, the specification exemplifies details on "cyclisation" reactions (see, e.g., paragraph [0097]) and "removing" protecting groups (see, e.g., paragraph [0085]).

In re Appln. of Benjes et al.  
Application No. 10/615,044

In view of the foregoing, one of ordinary skill in the art can determine the metes and bounds of the pending claims. Therefore, Applicants request that the rejection under Section 112, second paragraph, is improper and should be withdrawn.

*Discussion of the Anticipation Rejection*

Claims 1-18 have been rejected under 35 U.S.C. § 102(b), as allegedly being anticipated by Kayakiri reference I and II, individually or together. To the extent that the rejection under Section 102(b) is founded on combining the references cited by the Examiner, Applicants contend that the rejection is improper. The Office asserts that Kayakiri reference I and II discloses all the elements of the claimed processes. This rejection is respectfully traversed.

Solely in an effort to advance prosecution of the subject application, and not in acquiescence of the rejection, claim 1 has been amended to recite that the nitrogen protecting group is *N*-acetyl, claims 6 and 7 have been amended to recite *N*-acetyl-D-mannosamine, and claim 8 has been amended to recite 6-*O*-protected-*N*-acetyl-D-mannitol. According to the Office, each of the Kayakiri references discloses a process for preparing kifunensine from D-mannosamine using oxamic acid, which produces an *N*-oxamoyl-protected-D-mannosamine intermediate. Neither reference cited by the Office Action describes a process which employs an *N*-acetyl nitrogen protecting group. Because neither of the cited references discloses the subject matter of the pending claims, the rejection under Section 102(b) should be withdrawn.

*Discussion of the Obviousness Rejection*

Claims 1-18 have been rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Kayakiri reference I, in view of Kayakiri reference II. The Office asserts that Applicants change the sequence of reaction steps or selectively combine steps and reagents from Kayakiri references I and II. The Examiner further contends that the cited references teach all the steps, reagents, and reaction conditions of the claimed process. This rejection is respectfully traversed as Applicants contend that the use of the *N*-acetyl protecting group is not disclosed in Kayakiri references I and II and is not obvious in view of the cited references.

Claim 1 has been amended to recite that the nitrogen protecting group is *N*-acetyl. Applicants have found, in contrast to Kayakiri reference I and II, that if an *N*-acetyl protecting group is used, as opposed to the *N*-oxamoyl protecting group employed in Kayakiri reference I and II, then problems associated with the cited references, for example,

In re Appln. of Benjes et al.  
Application No. 10/615,044

conducting the process on a large scale and irreproducibility in the silylation step, can be overcome (see, e.g., paragraph [0005]).

Kayakiri reference I and II do not disclose the use of an *N*-acetyl protecting group or its removal. Further, one of ordinary skill in the art would not have a reasonable expectation of success in using an *N*-acetyl protecting group, given the harsh conditions necessary for its removal (aqueous Ba(OH)<sub>2</sub> at elevated temperature and pressure, see paragraph [0086]). The skilled artisan would not predict that the compound as a whole would survive such conditions. Thus, it would not be obvious to one of ordinary skill in the art to use an *N*-acetyl protecting group, as opposed to an *N*-oxamoyl protecting group, to facilitate conducting the process on a large scale and the selective and reproducible introduction of an O-6 protecting group.

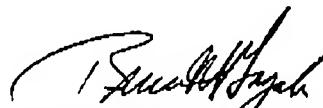
As such the claimed process overcomes the problems of scale up and irreproducibility in the O-protection step. For the reasons set forth above, one of ordinary skill in considering the cited references would not have been able to practice the invention defined by claim 1 and claim 17, and claims depending therefrom, with a reasonable expectation of success.

Accordingly, the Section 103 rejection should be withdrawn.

*Conclusion*

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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